REMARKS

I. Status

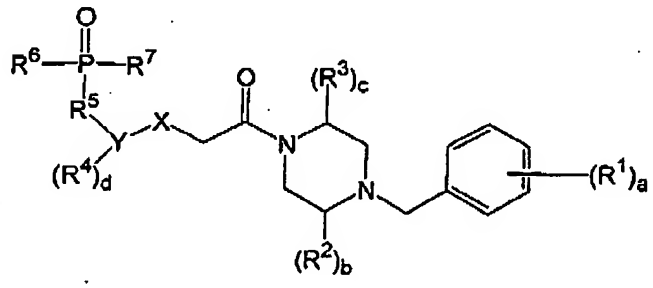
Claims 1-15 are pending in the application. Claims 1, 2, 8, 12, and 13 are currently amended to correct certain errors of a typographical nature, which were originally presented unintentionally and in good faith. No new matter is being presented by the current amendments.

Claims 1-15 stand rejected under 35 U.S.C. § 112, ¶1 with regard to enablement. Claims 11-15 stand rejected under 35 U.S.C. § 112, ¶2. The Examiner also discusses the potential for a double patenting rejection (presumably obviousness-type double patenting). Applicants respectfully traverse each of the rejections.

II. Claims 1-15 Are Enabled

Claims 1-15 stand rejected under 35 U.S.C. § 112, ¶1 with regard to enablement. Applicants respectfully traverse the rejection.

Claim 1 defines a compound of the Formula I



I

a prodrug thereof, or a pharmaceutically acceptable salt of the compound or the prodrug thereof, wherein the variables are defined. The presently disclosed compounds are selective inhibitors of MIP-1α (CCL3) binding to its receptor CCR1 found on inflammatory and immunomodulatory cells.

At page 2 of the Office Action, the Examiner asserts that the claims contain subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Applicants traverse the rejection at least because the specification adequately discloses how to make and use the claimed subject matter.

With regard to independent compound claim 1, the specification certainly discloses how to make the compounds defined by claim 1 at least because of the disclosed synthetic schemes and corresponding descriptions at pages 13-27. The Examiner does not appear to disagree in this regard. Rather, the Examiner appears to believe that the specification does not enable how to use the compounds defined by claim 1 in view of the Examiner's assertion at page 5 of the Office Action, "The compounds have been included in the rejection as no viable utility for the compounds is noted."

Applicants believe the present rejection is improper because the Examiner has not rejected the cited claims under 35 U.S.C. § 101, thereby admitting that the compounds defined by the cited claims possess the requisite utility. As the Examiner knows, "the how to use prong of section 112 incorporates as a matter of law the requirement of 35 U.S.C. § 101 that the specification disclose as a matter of fact a practical utility for the invention." *Rasmusson et al. v. Smithkline Beecham Corp.*, 2005 U.S. App. LEXIS 12680, 12689-12690 (Fed. Cir. 2005) quoting *In re Cortwright*, 165 F.3d 1353, 1356 (Fed. Cir. 1999). Even if the present § 112, ¶1 rejection based on a "lack of utility" basis were proper, which it is not, the Examiner has not satisfied the burden of showing that the specification "suggests an inherently unbelievable undertaking or involves implausible scientific principles." *In re Cortwright*, 165 F.3d 1353, 1357 (Fed. Cir. 1999) quoting *In re Brana*,

51 F.3d 1560, 1566 (Fed. Cir. 1995). "Only after the PTO provides evidence showing that one of ordinary skill in the art would reasonably doubt the asserted utility does the burden shift to the applicant to provide rebuttal evidence sufficient to convince such a person of the invention's asserted utility." *In re Brana*, 51 F.3d 1560, 1566 (Fed. Cir. 1995). The Examiner evidently has not satisfied this burden because the Examiner has not indicated *with support* how the utility of the claimed inventions is implausible.

Further, the Examiner is respectfully reminded that the "PTO cannot make this type of rejection unless it has reason to doubt the objective truth of the statements contained in the written description." *In re Cortwright*, 165 F.3d 1353, 1357 (Fed. Cir. 1999). Nevertheless, the Examiner here merely states *without* support, e.g., at page 3 of the Office Action, "The language merely describes applicants' intent for the compound. It is not clear that the claimed diseases, conditions, or disorders, are 'treated' via the claimed pathways." The Examiner further asserts at page 4 of the Office Action, "Applicants have not demonstrated that a single compound according to the invention can treat any disease, condition or disorder by inhibiting MIP-1α and/or RANTES from binding to the receptor CCR1..."

While not being obligated to respond further since the Examiner has apparently not satisfied the requisite burden of proof, it is worth mentioning that the present disclosure does indeed enable *inter alia* those of skill in the art to use the scope of compounds claimed. Applicants disclose the utility of the claimed compounds throughout the specification, e.g., at page 30, lines 17-18: "All of the compounds of the invention illustrated in the following examples had IC_{50} of less than 10μM, in the Chemotaxis assay." The specification also discloses a chemotaxis assay at page 29 that tests the functional effects of CCR1 and the CCR1 blockade. Further, the state of the art at the time of filing

was sufficient to establish a reasonable expectation that the inventions defined by the cited claims have a practical utility. Indeed, the specification, e.g., at page 1, discloses numerous publications linking MIP-1α binding to the CCR1 receptor and presently defined conditions or disorders. Certain of the publications of record also draw such a correlation. The combination of the state of the art and Applicants' present disclosure of IC_{50} values with corresponding chemotaxis assay certainly corroborates the indicated uses and demonstrates a "viable utility" contrary to the Examiner's assertion.

With regard to the pharmaceutical art, it is also important to distinguish between utility for patentability and utility for market entry, which the Examiner is apparently requiring. The Federal Circuit in *In re Brana* has made it clear that proof of an alleged pharmaceutical property for a compound by statistically significant tests with standard experimental results is sufficient to establish utility. *Brana* at 1567. The Court continued:

> FDA approval, however, is not a prerequisite for finding a compound useful within the meaning of the patent laws. *Scott*, 34 F.3d 1058, 1063, 32 U.S.P.Q.2D (BNA) 1115, 1120. Usefulness in patent law, and in particular in the context of pharmaceutical inventions, necessarily includes the expectation of further research and development. The stage at which an invention in this field becomes useful is well before it is ready to be administered to humans. Were we to require Phase II testing in order to prove utility, the associated costs would prevent many companies from obtaining patent protection on promising new inventions, thereby eliminating an incentive to pursue, through research and development, potential cures in many crucial areas such as the treatment of cancer. *In re Brana* at 1568.

"We hold as we do because it is our firm conviction that one who has taught the public that a compound exhibits some desirable pharmaceutical property in a standard experimental animal has made a significant and useful contribution to the art, even though it may eventually appear that the compound is without value in the treatment in humans." *Id* at 1567.

In view of the foregoing remarks, Applicants respectfully request reconsideration of the present rejection and its removal at this time.

III. Claims 11-15 Are Definite

Claims 11-15 stand rejected under § 112, ¶2. Applicants respectfully traverse the rejection.

In particular, the Examiner asserts at pages 5-6 of the Office Action that the various terms listed at pages 6-7 of the Office Action are unclear. At the outset, Applicants respectfully traverse the rejection because the Examiner appears to be using §112, ¶2 to bolster the §112, ¶1 enablement rejection discussed above, which is apparent from the Examiner's statement, "In addition, the intended coverage of scope encompassed those character and conditions that will be correlated to future discovery to be related to the diseases or conditions or disorders so named and as such is wholly inoperable."

The Examiner is respectfully reminded that the essential inquiry pertaining to the requirement under § 112, ¶2 is whether the claims set out and circumscribe a particular subject matter with a reasonable degree of clarity and particularity. Definiteness of claim language must be analyzed, not in a vacuum, but in light of: (A) the content of the particular application disclosure; (B) the teachings of the prior art; and (C) the claim interpretation that would be given by one possessing the ordinary level of skill in the pertinent art at the time the invention was made. M.P.E.P § 2173.02 (8th ed.).

Here, those of skill in the art given the benefit of the present disclosure would certainly understand the meaning of the cited terms. For instance, those of skill in the art considering the phrase "treating a condition mediated by inhibiting the MIP-1α and/or RANTES from binding to the

receptor CCR1" would have an appreciation as to the identity of such conditions, especially in view of Applicants' disclosure at page 1. Similarly, those of skill in the art given the benefit of the present disclosure appreciate the meaning of cited terms: autoimmune diseases (specifically taught, e.g., at page 12, lines 10-13; inflammatory conditions (specifically taught, e.g., at page 12, lines 24-28); gastrointestinal inflammation (specifically taught, e.g., at page 13, line 12).

In view of the foregoing remarks, claims 11-15 are definite and an indication to that effect is respectfully requested at this time.

IV. Double Patenting

At page 6 of the Office Action, the Examiner discusses certain differences between the presently defined compounds and the following pending applications: United States Serial Nos. 10/198,237 (published as US 2003/0181352); 10/346,684 (published as US 2003/0176447); 10/759,562 (published as US 2004/0176383); and 10/759,555 (published as US 2004/0186109). The Examiner then concludes, "no double patenting rejection will be made."

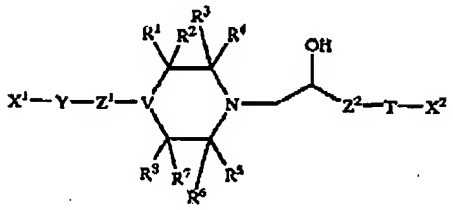
Aside from the merits of the Examiner's discussion, Applicants note that a double patenting rejection is inappropriate here because the pending application and the cited applications are not commonly owned, subject to an assignment to a common assignee, or have the same inventive entity. The present application is assigned to Pfizer Inc. whereas the referenced U.S. applications appear to be assigned to CV Therapeutics, which is not an entity related to Pfizer Inc. Before consideration can be given to the issue of double patenting, there must be some common relationship of inventorship and/or ownership of two or more patents or applications. M.P.E.P. § 804 (8th ed.).

While not expressly raised by the Examiner, it is worth mentioning that the compounds defined by claim 1 are patentable over the cited applications with regard to 35 U.S.C. § 103(a). At the outset, Applicants contend that USSN 10/759,555 is not prior art under § 102 and therefore cannot be prior art under § 103(a) because the only potential available section of § 102 available is § 102(e)(1). The § 102(e)(1) date of USSN 10/759,755 is January 17, 2003, which is after Applicants' priority date under 35 U.S.C. § 119(e) of December 13, 2002. In addition, USSN 10/759,562 and USSN 10/346,684 are potentially available as prior art under § 102(e)(1) and therefore under § 103 only to the extent that the subject matter it discloses is supported by priority application USSN 60/306,621 filed July 19, 2001 because other priority dates of these applications are after Applicants' priority date. Since USSN 10/759,562 is a continuation in part of USSN 10/346,684, which in turn is a continuation in part of USSN 10/198,237, which claims priority to USSN 60/306,621, it is reasonable to believe that both USSN 10/759,565 and USSN 10/346,684 are cumulative of USSN 10/198,237 for prior art purposes here. As such, only USSN 10/198,237 is discussed below.

Claim 1 is not *prima facie* obvious in view of USSN 10/198,237 ("the '237 application") at least because the '237 application does not teach or suggest each and every element of claim 1. For instance, the '237 application does not teach at least the $[(R^6R^7\text{-}(P{=}O)\text{-}R^5\text{-})((R^4)_d)]Y\text{-}X\text{-}CH_2\text{-}(C(O))\text{-}$ moiety of Applicants' formula I shown above. As discussed herein, the disclosed compounds are selective inhibitors of MIP-1α (CCL3) binding to its receptor CCR1 found on inflammatory and immunomodulatory cells and are potentially useful in part for the treatment or prevention of certain autoimmune diseases.

In contrast, the '237 application discloses at claim 1 a compound of the formula:

Formula I



wherein the definitions of X^1-Y^1-Z^1 do not correspond with Applicants' formula I. Indeed, the definitions are drastically different from Applicants' formula I. In just one example, Z^1 is defined as being optionally substituted alkylene of 1-4 carbon atoms, whereas a corresponding position of Applicants' formula is a carbonyl group (C=O). In addition, the group immediately adjacent to the nitrogen atom in Formula I of the '237 application is a methylene group, which, of course, does not correspond with the aforementioned carbonyl group. Further, the '237 application does not teach or suggest a modification to arrive at the presently defined carbonyl group.

In addition, the '237 application teaches at the Abstract that its heterocyclic derivatives are useful for the treatment of cardiovascular diseases such as atrial and ventricular arrhythmias, intermittent claudication, etc. The '237 application does not teach and in no way suggests compounds that inhibit MIP-1α (CCL3) binding to its receptor CCR1. Absent a teaching or suggestion, there is no reasonable expectation of success.

In view of the foregoing remarks, a potential rejection under § 103(a) over the cited applications would be overcome.

V. Conclusion

Having addressed all outstanding issues, Applicants kindly request removal of all rejections and allowance of all pending claims at this time. To the extent the Examiner believes that it would facilitate allowance of this case, the Examiner is urged to call the undersigned at the number below.

Applicants believe that no fee is associated with the filing of this paper. However, to the extent a fee is due, the Commissioner is hereby authorized by this paper to charge any required fees or credit any overpayment to Deposit Account 16-1445.

Respectfully submitted,

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